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| <u>L3</u> | L2 and 424/450.ccls. | 271 | <u>L3</u> |
| <u>L2</u> | liposome same (\$cancer or \$neoplastic or \$tumor) same gene | 2976 | <u>L2</u> |
| <u>L1</u> | liposome same (taxol or taxane or camptothecin) same gene | 67 | <u>L1</u> |

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L1: Entry 64 of 67

File: USPT

Dec 15, 1998

DOCUMENT-IDENTIFIER: US 5849727 A

TITLE: Compositions and methods for altering the biodistribution of biological agents

Brief Summary Text (5):

To date, drug delivery systems have included drug carriers based upon proteins, polysaccharides, synthetic polymers, erythrocytes, DNA and liposomes. New generation biologicals such as monoclonal antibodies, gene therapy vectors, anti-cancer drugs such as Taxol, viral based drugs, and oligo and poly nucleotides have presented several problems with regard to delivery. In fact drug delivery may be the primary hurdle to achieving mainstream therapeutic use of these biologics whose initial potential seemed unlimited but whose therapeutic parameters have prevented realization of full benefit.

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L3: Entry 213 of 271

File: USPT

Jan 9, 2001

DOCUMENT-IDENTIFIER: US 6171614 B1

**** See image for [Certificate of Correction](#) ****

TITLE: Synthesis of glycopospholipid and peptide-phospholipid conjugates and uses thereof

Detailed Description Text (55):

Liposomes can also be modified to contain surface-associated targeting information whereby resultant liposomes can be made specific for a designated cell type or tissue. For example, site-directing targeting ligands, such as monoclonal antibodies, can be attached to liposomes either covalently or non-covalently [Allen (1994) Trends Pharmacol. 15:215-220; Laukkanen et al. (1994) Biochemistry 33:11664-11670]. To date, antibodies [Lee et al. (1994) J. Biol. Chem. 269:3198-3204; Blume et al. (1993) Biochim. Biophys. Acta 1149:180-184; Maruyama et al. (1995) Biochim. Biophys. Acta 1234:74-80; and Allen et al. (1995) Biochim. Biophys. Acta 1237:99-108], glycolipids, e.g., galactose [Van Berkel et al. (1993) in Liposome Technology, Vol. 3, Edition 2 (Gregoriadis, ed.), CRC Press, Boca Raton, pp. 219-230] and mannose [Barratt et al. (1993) in Liposome Technology, Vol. 3, Edition 2 (Gregoriadis, ed.) CRC Press, Boca Raton, pp. 199-218], proteins, e.g., transferrin [Stavridis et al. (1986) Exp. Cell Res. 164:568-572] and asialofetuin [Hara et al. (1995) Gene 159:167-174], and vitamins, e.g., folic acid [Lee et al. (1995) Biochim. Biophys. Acta 1233:134-144] have been used to target specific cells via cell surface receptors. Also, improved therapeutic activity of liposomal drugs was obtained through the use of antibody-mediated targeting [Ahmad et al. (1993) Cancer Res. 53:1484-1488; Mori et al. (1995) Cancer Chemother. Pharmacol. 35:447-456].

Detailed Description Text (58):

Glycopospholipid- and peptide-phospholipid-liposomes of the present invention can also be used to formulate a pharmaceutical composition useful for diagnosis, therapy, drug delivery, gene therapy, and other such indications. Such pharmaceutical compositions comprising glycopospholipid or peptide-phospholipid conjugates and a pharmaceutically acceptable carrier are effective in the therapeutic treatment of diseases, such as cancer, thrombosis, etc.

Current US Original Classification (1):

424/450

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L3: Entry 218 of 271

File: USPT

Aug 29, 2000

US-PAT-NO: 6110490

DOCUMENT-IDENTIFIER: US 6110490 A

TITLE: Liposomal delivery system for biologically active agents

DATE-ISSUED: August 29, 2000

INVENTOR-INFORMATION:

| NAME | CITY | STATE | ZIP CODE | COUNTRY |
|-------------------|------------|-------|----------|---------|
| Thierry; Alain R. | Strasbourg | | | FR |

US-CL-CURRENT: 424/450; 424/400

CLAIMS:

What is claimed is:

1. A composition comprising a bi- or multi-layer membrane surrounding an internal aqueous liposome comprising at least one cationic lipopolyamine and at least one neutral lipid provided in a molar ratio range said ratio from about 0.02:1 to about 2.0:1.
2. A composition according to claim 1 wherein the lipopolyamine comprises a quaternary or tertiary polyamine lipid.
3. A composition according to claim 2 wherein at least one cationic lipopolyamine is selected from the group consisting of 2,3-dioleyloxy-N[2 (sperminecarboxamido)ethyl]-N,N-dimethyl-1-propanaminium trifluoroacetate, N[1-(2,3-dioleyloxy) propyl]-N,N,N-trimethyl-ammonium chloride and Spermine-5-carboxy-glycinediotadecylamide.
4. A composition according to claim 3 wherein the cationic lipopolyamine comprises at least one spermine-5-carboxy-glycinedioctadecylamide.
5. A composition according to claim 1 wherein the neutral lipid is a neutral amino phospholipid.
6. A composition according to claim 5 wherein the neutral lipid is selected from the group consisting of dioleoylphosphatidyl ethanolamine and phosphatidylethanolamine.
7. A composition of claim 1 wherein the cationic lipopolyamine comprises spermine-5-carboxy-glycinedioctadecylamide and the neutral lipid comprises dioleoylphosphatidyl ethanolamine.
8. A composition of claim 1 wherein the cationic lipopolyamine comprises

spermine-5-carboxy-glycindiocetadecylamide and the neutral lipid comprises phosphatidylethanolamine.

9. A composition according to claim 1 or 7 further comprising a biologically active agent.

10. A composition according to claim 9 wherein the biologically active agent is selected from the group consisting of a therapeutic agent, a protein or a nucleic acid.

11. A composition according to claim 10 wherein the nucleic acid is selected from the group consisting of a chromosome of a chromosomal fragment, a deoxyribonucleic acid, a ribonucleic acid, a ribozyme, an oligonucleotide, an anti-sense oligonucleotide, a plasmid DNA or a nucleic acid viral in origin.

12. A method of preparing a liposome comprising the steps of:

(a) mixing a cationic lipopolyamine with a neutral lipid in a molar ratio range of about 0.02:1 to about 2.0:1, forming a mixture;

(b) evaporating the mixture to dryness, forming a dried film;

(c) adding a biologically active agent;

(d) rehydrating the dried film with said biologically active agent forming the liposome.

13. The method of claim 12 wherein the biologically active agent is a nucleic acid solution provided in a ratio of 40-240 microgram nucleic acid per milligram lipid.

14. The method of claim 13 wherein said nucleic acid is provided in a concentration of about 1-3 mg/ml.

15. The method of claim 13 further comprising rehydrating the dried film in a solution having a pH of 5.5-6.5.

16. The method of claim 13 wherein the aqueous solution is water.

17. A method of introducing a biologically active agent into cells of a subject comprising administering to the subject an effective amount of a composition according to claim 9.

18. The method of claim 17 wherein the biologically active agent is a nucleic acid.

19. The method of claim 18 wherein the nucleic acid is a DNA.

20. A composition of claim 9 wherein the biologically active agent comprises adenovirus particles.

21. A composition according to claim 9 further comprising adenovirus particles.

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L3: Entry 225 of 271

File: USPT

May 2, 2000

DOCUMENT-IDENTIFIER: US 6056973 A

TITLE: Therapeutic liposome composition and method of preparation

Detailed Description Text (93):

Continuing with the example of using the library for treatment of human breast cancer, the library further includes a therapeutic liposome composition or a plurality of liposome compositions containing encapsulated agents appropriate for treating human breast cancer cells in vivo. The pre-formed liposomes are in the form of pre-filled vials containing the liposomes as a sterile suspension in appropriate buffers is created. Liposome containing the following entrapped agents are exemplary for the human breast cancer example: doxorubicin, cisplatin, water-soluble camptothecin derivatives (e.g. topotecan, navelbine, vincristine, antisense oligonucleotides, p53 gene, HSVtk gene, a radiation sensitizer and an angiogenesis inhibitor.

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